

## General

### Guideline Title

Guideline: updates on HIV and infant feeding: the duration of breastfeeding, and support from health services to improve feeding practices among mothers living with HIV.

### Bibliographic Source(s)

World Health Organization (WHO), United Nations Children's Fund (UNICEF). Guideline: updates on HIV and infant feeding: the duration of breastfeeding, and support from health services to improve feeding practices among mothers living with HIV. Geneva (Switzerland): World Health Organization (WHO); 2016. 58 p. [52 references]

### Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: World Health Organization (WHO). Guidelines on HIV and infant feeding. Geneva (Switzerland): World Health Organization (WHO); 2010. 49 p. [47 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Recommendations

### Major Recommendations

*Note from the National Guideline Clearinghouse (NGC):* See Table 3 in the original guideline document for principles and recommendations from the 2010 guidelines on human immunodeficiency virus (HIV) and infant feeding, which, as stated by the World Health Organization (WHO), remain valid except as noted.

The definitions for the strength of the recommendations (strong, conditional, no recommendation) and the quality of evidence (high, moderate, low, very low) are provided at the end of the "Major Recommendations" field.

#### The 2016 WHO Recommendations on HIV and Infant Feeding

Recommendation 1. The Duration of Breastfeeding by Mothers Living with HIV<sup>a</sup>

*For how long should a mother living with HIV breastfeed if she is receiving antiretroviral therapy (ART) and there is no evidence of clinical, immune or viral failure?*

Mothers living with HIV should breastfeed for at least 12 months and may continue breastfeeding for up to 24 months or longer (similar to the general population) while being fully supported for ART adherence (see the WHO consolidated guidelines on ARV drugs for interventions to

optimize adherence).<sup>b</sup> (Strong recommendation, low quality of evidence [for 12 months] and very low quality of evidence [for 24 months])

The Guideline Development Group agreed that Recommendation 1 should be framed by the following statement:

In settings where health services provide and support lifelong ART, including adherence counselling, and promote and support breastfeeding among women living with HIV, the duration of breastfeeding should not be restricted.

"Mothers known to be HIV-infected (and whose infants are HIV uninfected or of unknown HIV status) should exclusively breastfeed their infants for the first six months of life, introducing appropriate complementary foods thereafter and continue breastfeeding."

"Breastfeeding should then only stop once a nutritionally adequate and safe diet without breast milk can be provided."

<sup>a</sup>This recommendation updates the component of the 2010 recommendation on which breastfeeding practices and for how long related to the duration of breastfeeding. The components of the 2010 recommendation regarding breastfeeding practices and stopping breastfeeding remain unchanged and valid.

<sup>b</sup>WHO-recommended breastfeeding is defined as: (1) initiation of breastfeeding within the first hour of life; (2) exclusive breastfeeding for the first six months of life (that is, the infant only receives breast milk without any additional food or drink, not even water); followed by (3) continued breastfeeding for up to two years of age or beyond (with the introduction of appropriate complementary foods at six months); and (4) breastfeeding on demand – that is, as often as the child wants, day and night.

## Recommendation 2. Interventions to Support Infant Feeding Practices by Mothers Living with HIV

*Can facility- and community-based interventions improve the quality of infant feeding practices among mothers living with HIV?*

National and local health authorities should actively coordinate and implement services in health facilities and activities in workplaces, communities and homes to protect, promote and support breastfeeding among women living with HIV. (Strong recommendation, high quality of evidence)

### 2016 Guiding Practice Statements

#### Practice Statement 1. When Mothers Living with HIV Do Not Exclusively Breastfeed

*If a mother living with HIV does not exclusively breastfeed, is mixed feeding with ART better than no breastfeeding at all?*

Mothers living with HIV and health-care workers can be reassured that ART reduces the risk of postnatal HIV transmission in the context of mixed feeding. Although exclusive breastfeeding is recommended, practising mixed feeding is not a reason to stop breastfeeding in the presence of ARV drugs.

#### Practice Statement 2. When Mothers Living with HIV Do Not Plan to Breastfeed for 12 Months

*If a mother living with HIV plans to return to work or school, is a shorter duration of planned breastfeeding with ART better than no breastfeeding at all?*

Mothers living with HIV and health-care workers can be reassured that shorter durations of breastfeeding of less than 12 months are better than never initiating breastfeeding at all.

### Definitions

#### Criteria for Assessing the Strength of the Recommendations

Strength of the Recommendation	Rationale
Strong	<p>The Guideline Development Group is confident that the desirable effects of adherence to the recommendation outweigh the undesirable effects.</p> <p>With strong recommendations, the guideline communicates the message that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that, in most situations, the recommendation can be adopted as policy.</p>
Conditional	<p>The Guideline Development Group concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects. However, the recommendation is only applicable to a specific group, population or setting or where new evidence may result in changing the balance of risk to benefit or where the benefits may not warrant the cost or resource requirements in all settings.</p> <p>Conditional recommendations are made when there is greater uncertainty about the benefits versus risks, values and preferences, feasibility and acceptability and cost, or if local adaptation has to account for a greater variety in values and</p>

<b>Strength of the Recommendation</b>	<b>Rationale</b>
No recommendation	preferences or when resource use makes the intervention suitable for some locations but not for others. This means that substantial debate and involvement of stakeholders are needed before this recommendation can be adopted as policy. Further research is required before any recommendation can be made.

Definition of the Quality of the Evidence Using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Method

Grade	Definition	Implication
High	The Guideline Development Group is very confident that the true effect lies close to that of the estimate of the effect.	Further research is very unlikely to change confidence in the estimate of the effect.
Moderate	The Guideline Development Group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	Further research is likely to have an important impact on confidence in the estimate of the effect and may change the estimate.
Low	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect.	Further research is very likely to have an important impact on confidence in the estimate of the effect and is unlikely to change the estimate.
Very low	The Guideline Development Group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.	Any estimate of effect is very uncertain.

## Clinical Algorithm(s)

None provided

## Scope

## Disease/Condition(s)

- Human immunodeficiency virus (HIV) infection
- Infant health and nutritional status

## Guideline Category

Counseling

Management

Prevention

Risk Assessment

Treatment

## Clinical Specialty

Family Practice

Infectious Diseases

Internal Medicine

Nursing

Nutrition

Obstetrics and Gynecology

Pediatrics

Preventive Medicine

## Intended Users

Advanced Practice Nurses

Allied Health Personnel

Dietitians

Health Care Providers

Nurses

Other

Physician Assistants

Physicians

Public Health Departments

## Guideline Objective(s)

- To improve the human immunodeficiency virus (HIV)-free survival of HIV-exposed infants by providing guidance on appropriate infant feeding practices and use of antiretroviral (ARV) drugs for mothers living with HIV and by updating World Health Organization (WHO)-related tools and training materials
- To help Member States and their partners in their efforts to make informed decisions on the appropriate nutrition actions to achieve the Sustainable Development Goals, the global targets set in the comprehensive implementation plan on maternal, infant and young child nutrition, the Global Strategy for Women's, Children's and Adolescents' Health (2016–2030) and the Global Health Sector Strategy on Sexually Transmitted Infections 2016–2021

## Target Population

Human immunodeficiency virus (HIV)-positive mothers receiving antiretroviral therapy (ART) and their infants (breastfed, partially breastfed, or receiving breast milk substitutes such as formula)

Note: The guideline is intended mainly for countries with high HIV prevalence and settings in which diarrhoea, pneumonia and undernutrition are common causes of infant and child mortality. However, it may also be relevant to settings with a low prevalence of HIV depending on the background rates and causes of infant and child mortality.

## Interventions and Practices Considered

1. Duration of breastfeeding by mothers living with human immunodeficiency virus (HIV)
2. Interventions to support infant feeding practices by mothers living with HIV
3. Advice for mothers living with HIV who do not exclusively breastfeed (mixed feeding versus no breastfeeding)
4. Advice for mothers living with HIV who do not plan to breastfeed for 12 months (shorter duration of planned breastfeeding versus no breastfeeding)

## Major Outcomes Considered

- Human immunodeficiency virus (HIV)-free survival between birth and 24 months
- HIV transmission rate
- Adherence of HIV-infected mothers to antiretroviral therapy
- Exclusive breastfeeding (at 3 months and 6 months)
- Initiation of breastfeeding
- Early initiation of breastfeeding (within 1 hour of birth)
- Safe replacement feeding
- Infant mortality

## Methodology

### Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

### Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse: The World Health Organization (WHO) examined 3 systematic reviews (see the "Availability of Companion Documents" field).

HIV-Free Survival at 12–24 Months in Breastfed Infants of HIV-Infected Women on ART: a Systematic Review

Inclusion Criteria

*Types of Studies*

The review considered both experimental and observational studies e.g., randomised control studies (RCTs), cohort studies, and longitudinal studies, and included HIV-positive mothers receiving antiretroviral (ARV) therapy and their breastfed children. Infants may also have received prophylactic ARVs as per WHO 2010 guidelines.

*Types of Participants*

HIV-positive mothers receiving combined ART and their breastfed children.

*Types of Exposures*

HIV ART (and duration) and breastfeeding (and duration).

*Outcome Measures*

The outcome measures were HIV-free survival and HIV transmission between birth and 24 months of age.

Search Strategy

One reviewer searched English literature from multiple electronic databases including PubMed, MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Web of Science, and CINAHL for articles with a time limit of 2005 to 2015 (see Table 1 in the systematic review). The search words in PubMed are shown in Table 2 and more detailed in Appendix 1 of the review.

The reviewer did the initial search of literature in discussion with the two other reviewers. The search terms were adapted for other databases. Reference lists from relevant studies, grey literature and conference abstracts available online from the following conferences were also searched: the International IAS (International AIDS Society) AIDS Conference in Melbourne 2014 and the 2013-2015 Conferences on Retroviruses and Opportunistic Infections (CROI). The reference lists of articles identified from the search of databases and conference abstracts were further

searched. Also, in some cases where relevant information was not available in the publication, authors were contacted for specific additional information regarding infant feeding modality (data collection and support). Seven questions were asked of 10 first authors, additional information provided is included in the second systematic review which focussed on HIV transmission and infant feeding modality in the first six months of life.

### Postnatal HIV Transmission Rates at Age Six and 12 months in Infants of HIV-Infected Women on ART Initiating Breastfeeding: a Systematic Review of the Literature

#### *Inclusion Criteria*

#### *Types of Studies*

The review considered both experimental and observational studies e.g., randomised control studies, cohort studies and longitudinal studies, and included HIV-positive mothers receiving ART and their breastfed children. Infants may also have received prophylactic ARVs as per WHO 2010 guidelines.

#### *Types of Participants*

HIV-positive mothers receiving ART from before or early pregnancy until at least 6 months postpartum and their breastfed children.

#### *Types of Exposures*

The exposures were HIV ART and feeding modality during breastfeeding (exclusive breastfeeding, mixed feeding).

#### *Outcome Measures*

The outcome measures were overall HIV transmission rate between birth and 6 months of age, and postnatal transmission rate between 4-6 weeks and 6 months, and overall and postnatal transmission rates at 12, 18 or 24 months, as provided by the study.

#### *Search Strategy*

See the "Search Strategy" for the first review above. See the systematic review for minor differences.

To obtain further information for this and the first systematic review, the reviewers contacted ten first authors of papers identified in the first systematic review, to solicit additional information regarding infant feeding modality in the first six months of life. Seven questions were asked: 1) What feeding practice did the study team recommend to HIV-infected mothers? 2) If breastfeeding, for how long were HIV-infected mothers recommended to breastfeed? 3) What type of support was provided to mothers to assist them in their feeding practice (e.g. frequency of counselling before and after delivery, facility or community-based, home visits, skill of counsellors, support provided if mother encountered difficulties, availability of free formula milk)? 4) How was data regarding infant feeding practices collected e.g. self-reporting, use of feeding diaries, frequency of interviews, independent field team? 5) Were feeding practices disaggregated in the study database, i.e., mixed feeding, exclusive breastfeeding? Was feeding type (exclusive vs. mixed feeding) included within a model examining postnatal transmission risk in the context of ARVs? 6) If feeding practices were characterised in the database, how were exclusive breastfeeding rates estimated, i.e., a cross-sectional practice at, e.g., 4 or 5 months, or estimated as cumulative practices determined by considering all data from birth? 7) What proportion of HIV-infected women in the study were truly exclusively breastfeeding at 4-6 months – is this from actual data or is this more of an impression from staff in the field?

### Systematic Review of Effectiveness of Interventions to Promote Exclusive Breastfeeding in Women That Are HIV(+) on Anti-retroviral Therapy Living in Areas That Promote Exclusive Breastfeeding Due to Limited Resources for Safe Replacement Feeding

#### *Research Question*

In HIV+ women on ART living in developing countries, what is the effectiveness of any breastfeeding promotion interventions compared to no interventions on initiation of breastfeeding and exclusive breastfeeding (for 3 months and 6 months)?

#### *Studies Included for This Review*

During the literature search phase there were no restrictions applied to study designs. Both randomized clinical trials assessing interventions that promoted early initiation and/or exclusive breastfeeding in the HIV/acquired immunodeficiency syndrome (AIDS) population as well as other nonrandomized clinical trials and intervention cohorts that provided data on early breastfeeding initiation (within one hour of birth), breastfeeding initiation, and exclusive breastfeeding at any time point were included in this review. Studies not published in English were excluded from the analysis.

## *Types of Participants*

Pre- and post-gestational HIV (+) women on ARV therapy

## *Types of Interventions*

- Group counseling
- Individual counseling sessions
- Staff training
- Community support
- Work environment support
- Policy environment
- Prenatal and postnatal education and counseling

## *Types of Outcomes Measured*

The following outcomes in HIV-exposed infants were assessed:

### Primary Outcomes

- Exclusive breastfeeding (3 months and 6 months)
- Initiation of breastfeeding
- Early initiation of breastfeeding (within 1 hour of birth)

## Search Methods for Identification of Studies

An intensive electronic search was conducted to answer the proposed questions. The authors of the review followed the search strategy as outlined by the Academy of Nutrition and Dietetics Evidence Analysis methodology.

Electronic databases searched included PubMed and EBSCO Search (MEDLINE, CINAHL, Food Science, Sport Discuss, EMBASE, and the EBSCO Discovery Service [EDS] databases).

First, the reviewers independently reviewed the list of titles and abstracts and selected those that met inclusion criteria. Next, the authors independently conducted a second round of review where the title and abstracts were further scrutinized. Articles were marked for inclusion or exclusion (along with reason); any differences were resolved by discussion with the third reviewer. The second review results were then categorized based on the following: review articles, qualitative articles, descriptive studies and clinical trial articles that examined the interventions and outcomes of interest. The reference list of review articles were hand searched for articles that met inclusion, then categorized as above. Full texts of studies selected for inclusion were ordered. A final list of included articles was developed after review of all ordered full text articles.

Attachment A in the systematic review provides information on the search strategy and full protocol.

## Search Results

Initial screening identified 859 citations; of these, 71 potentially relevant articles that met the inclusion and exclusion criteria were identified (see Figure 1 in the systematic review). After reviewing, 58 articles were excluded from the systematic review for the following reasons (see Appendix A of the review for detail explanation of exclusion):

- Review articles
- Data on outcomes of interest was not reported
- Population was not HIV positive
- Impact of intervention was not evaluated
- Information only on intention to breastfeed

## Number of Source Documents

### Human Immunodeficiency Virus (HIV)-Free Survival at 12–24 Months in Breastfed Infants of HIV-Infected Women on Antiretroviral Therapy (ART): a Systematic Review

The search process identified 1295 citations, of which 1139 were excluded on the basis of being a duplicate, review, qualitative study or not

evaluating transmission, mortality or HIV-free-survival. Eighteen studies were included in the analysis; eight additional papers from selected studies provided additional information for the assessment of quality of studies and data collection. See Figure 2 in the systematic review (see the "Availability of Companion Documents" field) for a flow chart of the screening process.

#### Postnatal HIV Transmission Rates at Age Six and 12 Months in Infants of HIV-Infected Women on ART Initiating Breastfeeding: a Systematic Review of the Literature

The search process identified 1,439 citations, of which 1,367 were excluded on the basis of being a duplicate, review, qualitative study or not evaluating transmission at six months according to feeding modality. No studies were identified in addition to the first systematic review on HIV-free survival (see above). Eleven studies included in the first review were also analysed in this review. See Figure 1 in the systematic review for a flow chart of the screening process.

#### Systematic Review of Effectiveness of Interventions to Promote Exclusive Breastfeeding in Women That Are HIV(+) on Anti-retroviral Therapy Living in Areas That Promote Exclusive Breastfeeding Due to Limited Resources for Safe Replacement Feeding

Initial screening identified 859 citations; of these, 71 potentially relevant articles that met the inclusion and exclusion criteria were identified. After reviewing, 58 articles were excluded from the systematic review for the following reasons. Thirteen articles were included in the review. See Figure 1 in the systematic review for a flow chart of the screening process.

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

### Rating Scheme for the Strength of the Evidence

Definition of the Quality of the Evidence Using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Method

Grade	Definition	Implication
High	The Guideline Development Group is very confident that the true effect lies close to that of the estimate of the effect.	Further research is very unlikely to change confidence in the estimate of the effect.
Moderate	The Guideline Development Group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	Further research is likely to have an important impact on confidence in the estimate of the effect and may change the estimate.
Low	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect.	Further research is very likely to have an important impact on confidence in the estimate of the effect and is unlikely to change the estimate.
Very low	The Guideline Development Group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.	Any estimate of effect is very uncertain.

## Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

### Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse: The World Health Organization (WHO) examined 3 systematic reviews. As additional evidence not included in the evidence tables for this guideline, findings are presented of a modelling exercise that was also commissioned for the guideline and examined the effect of antiretroviral therapy (ART) among mothers living with human immunodeficiency virus (HIV) on infant survival according to different background risk assessments of diarrhoeal mortality (see the "Availability of Companion Documents" field).

## HIV-Free Survival at 12–24 Months in Breastfed Infants of HIV-Infected Women on ART: a Systematic Review

### Assessment of Quality of Studies

#### *Newcastle-Ottawa Scale*

The reviewers developed a modified Newcastle-Ottawa Scale (NOS) to assess the quality of all studies included in the analysis; the criteria for assessment of the quality of studies are provided in Appendix 4, with the detailed NOS table in Appendix 5 of the systematic review. Although some of the included studies were nested within randomised controlled trials (RCTs), randomisation was not based on the intervention of interest (breastfeeding) and these studies were considered cohorts. Stars were awarded for each study based on selection of study participants and assessment of outcomes; assessment did not use all aspects of the NOS because the papers included in this research only assessed human immunodeficiency virus (HIV)-free survival in breastfed children whose mothers were on antiretroviral therapy (ART), and did not include a comparison group. Each study could score a maximum of six stars on Selection and four on Outcome. The factors considered included the representativeness of the study population in terms of the underlying population of HIV-positive pregnant women accessing prevention of mother-to-child transmission (PMTCT) programme, ascertainment of exposure to ART and breastfeeding, the basis of the ART in terms of HIV-disease progression, report of maternal adherence to ART and duration of breastfeeding. Ascertainment of outcome (HIV-free survival) included timing of assessment and whether the outcome was stratified by feeding, length of follow up and loss to follow up.

#### Grading of Recommendations Assessment, Development and Evaluation (GRADE)

The information obtained from the NOS was used to comment on the quality of the included studies in GRADE with respect to study limitations/risk of bias. Reviewers also considered consistency of results, directness and publication bias.

#### GRADE Profile

An evaluation of the quality of the studies considered in the analysis is given in Table 4 of the systematic review. The assessment of quality was based on study limitations/risk of bias as per the evidence from the Newcastle-Ottawa Scale (Table 3, Appendix 5 of the systematic review). We also considered inconsistency, indirectness and publication bias. Initially, all studies were scored low quality due to being observational and were downgraded for indirectness because their research areas were not directly in line with the PICO (population, intervention, control, outcome) question. Where a pooled analysis was undertaken and a pooled estimate provided, studies were further downgraded for inconsistency. In all groups of studies there was at least one study with a risk of bias pertaining to lack of detailed information on feeding leading to further downgrading (see Appendix 4 in the systematic review).

#### Synthesis of Evidence

The studies covered different types of interventions and varied with regard to the outcomes of interest of indication, timing of initiation and duration of maternal ART, breastfeeding recommendations and practice.

The reviewers present the evidence using a narrative synthesis, in addition to a pooled estimate with a heterogeneity score based on a random effects meta-analysis in Stata. Random effects meta-analysis is recommended for use in the analysis of studies that were conducted differently. The pooled estimate therefore represents the average estimate of HIV-free survival across the studies included in the analysis. The information in graphs depicting HIV-free survival rates by duration of maternal ART was summarised where possible, and additionally, HIV transmission rates were presented for studies which provided transmission rates at six months and at the end of follow-up. For most cases confidence intervals for estimates of HIV-free survival and/or HIV transmission were given; where no confidence interval was available from the paper, a confidence interval was calculated based on the number of events and those at risk using the formula described by Eayres and shown in Appendix 6 in the systematic review. To enable appropriate comparison of HIV-free survival between exclusively breastfed and formula-fed children the reviewers computed confidence intervals of the difference in the proportion of HIV-free survival between the two groups.

## Postnatal HIV Transmission Rates at Age Six and 12 months in Infants of HIV-Infected Women on ART Initiating Breastfeeding: a Systematic Review of the Literature

See the methodology above. See the systematic review for minor differences.

## Systematic Review of Effectiveness of Interventions to Promote Exclusive Breastfeeding in Women That Are HIV(+) on Anti-retroviral Therapy Living in Areas That Promote Exclusive Breastfeeding Due to Limited Resources for Safe Replacement Feeding

### Data Extraction and Management

Data was extracted using a standardized online data extraction tool. The following data was extracted from each included study:

- Study design
- Purpose of study
- Inclusion and exclusion criteria
- Country where study was performed
- Blinding
- Funding
- Size of sample population, dropout rate
- Age, ethnicity and gender of sample population
- Interventions studied: pre- or post-gestational population, group or individual counseling, intervention provider and setting, frequency and duration of intervention
- Outcomes measured: breastfeeding initiation, early breastfeeding initiation (within 1 hr of birth), exclusive breastfeeding with time point
- Quality criteria checklist (risk of bias): selection of participants free from bias, study groups comparable, methods of handling withdrawals, blinding, instruments valid and reliable, appropriate statistical analysis, potential bias and limitations

#### Assessment of Risk of Bias in Included Studies

Risk of bias was assessed according to the guidelines outlined in the *Cochrane Handbook for Randomized Controlled Studies*. The Newcastle-Ottawa Scale was used to assess risk of bias for observational studies. Randomized control study meeting the inclusion criteria were assessed according to the following:

- Sequence generation
- Allocation concealment
- Blinding
- Incomplete outcome data
- Selective outcome reporting
- Other sources of bias

The observational studies meeting the inclusion criteria were assessed according to the following:

- Selection of study groups
- Comparability of groups
- Ascertainment of exposure/outcome

The quality of each observational study was appraised using a "star system" and a scoring algorithm was used to classify the studies as Good, Fair, or Poor quality. Two reviewers independently evaluated the quality of studies and any differences were resolved with a third reviewer or by discussion.

Risk of bias for included studies is presented in Attachment B of the systematic review.

#### Data Analysis

Due to the heterogeneity of the studies in terms of study design, types of interventions, duration of interventions, methods, exposures, and outcomes it was not feasible to conduct a meta-analysis for this systematic review. Due to the same reasons as mentioned before, pooling of data was not possible. With the type of information available for these studies, narrative synthesis seemed the most appropriate method to present the findings. Synthesis focused on describing the intervention, direction of the findings, and overall results.

## Methods Used to Formulate the Recommendations

Expert Consensus (Consensus Development Conference)

## Description of Methods Used to Formulate the Recommendations

### Guideline Development Methods

The process outlined in the *World Health Organization (WHO) handbook for guideline development* was followed. This included: (1) identifying priority clinical questions and outcomes; (2) retrieving the evidence; (3) assessing the quality of evidence and synthesizing the findings; (4) formulating recommendations, including future research priorities; and (5) planning for dissemination, implementation, impact evaluation and

updating the guideline.

The Grading of Recommendations, Development and Evaluation (GRADE) method was followed to prepare evidence profile tables related to preselected topics, based on up-to-date systematic reviews. The Guideline Development Group comprised content experts, methodologists and representatives of potential stakeholder groups. Some of these experts participated in a WHO technical consultation held in New York City, United States of America, on 17–18 November 2014 to scope questions for the systematic reviews and guideline update.

The full Guideline Development Group met in Geneva, Switzerland on 21–23 October 2015, to review and discuss the evidence, draft the recommendations and agree on their strength, taking into consideration: (1) the desirable and undesirable effects of this intervention; (2) the quality (confidence in estimates of effect) of the available evidence; and (3) the values and preferences related to the intervention as well as to outcomes and specific contextual factors that pertain to various settings. The cost of the options available to health-care workers in various settings was not formally assessed because of lack of primary data in the literature or elsewhere, but the cost and resource implications were considered as part of a general discussion by the Guideline Development Group.

#### WHO Steering Committee

A Steering Committee, with members from the Department of Maternal, Newborn, Child and Adolescent Health, Department of Nutrition for Health and Development and the Department of HIV, has overseen the guideline review process. The acknowledgements list the WHO staff members on the Committee.

#### Guideline Development Group

WHO convened a 21-member Guideline Development Group consisting of internationally recognized experts in terms of content, methods and regional representation. Members were tasked with reviewing and evaluating the quality of the evidence identified through the systematic reviews using the GRADE method (described below) and revising and finalizing the guideline recommendations.

#### Decision-Making Process

For each draft recommendation, the WHO Steering Committee presented a synthesis of the evidence, the GRADE tables and the draft null recommendation language. The decision-making tables were drafted, including the benefits and risks of the interventions from a public health perspective; the values, preferences and acceptability to mothers living with HIV and their communities as well as programme managers, policy-makers and health-care providers; and the feasibility of implementing any recommendations (including the resources needed, focusing on national programmes in resource-limited or other settings).

Information from a survey of national health authorities from the 22 priority countries of the Global Plan (UNAIDS, 2011) and from an online survey of other stakeholders was used to inform the values and preferences (see Annex 3 in the original guideline document).

The cost of options available to health-care workers in various settings was not formally assessed because of a lack of primary data in the literature or elsewhere. However, the Guideline Development Group considered the cost implications as part of the general discussion. Comments were therefore restricted to personal experiences and extrapolations from general cost considerations of programmes.

Each Guideline Development Group member was asked to review the material and independently comment on and suggest revisions to the proposed guidance and decision-making tables. They were requested to rank the overall quality of the evidence using the GRADE method (independent of the rating made in the synthesis of the evidence), the balance of benefits versus harm, the values that should be considered in making a recommendation and the applicability of any proposed recommendations to the populations for whom they are intended. Finally, they were asked to assess what strength each recommendation should be given based on the criteria provided in "Rating Scheme of the Strength of the Recommendations" field.

The Guideline Development Group used a consensus-building process to finalize the recommendations. Once participants expressed their opinions and suggestions on a recommendation, the chairs and the WHO Steering Committee summarized this information. This summary was presented to the Guideline Development Group members to gauge the degree of consensus where differences existed. The chairs of the Guideline Development Group facilitated discussions among Guideline Development Group members until there was consensus on the language of each recommendation, the quality of the evidence and the strength. If consensus could not be reached, the Guideline Development Group had agreed at the beginning of the meeting that a simple majority vote would determine a contested decision.

WHO staff members did not express personal opinions on the data, in the discussions or in the decisions on language, the strength of the recommendations or the quality of the evidence. Throughout the meeting, WHO staff members articulated the principles and guidelines of the WHO decision-making process.

The Guideline Development Group reached agreement on all the recommendations following revisions of the text. The recommendations on the duration of breastfeeding by mothers living with human immunodeficiency virus (HIV) were discussed extensively to achieve consensus on the strength of the recommendation. Voting was only used as a straw-poll method to evaluate consensus, and no decisions were required to be subjected to a final vote.

The Guideline Development Group declined to make a recommendation in all cases, but instead formulated guiding practice statements using the same methods.

## Rating Scheme for the Strength of the Recommendations

### Criteria for Assessing the Strength of the Recommendations

Strength of the Recommendation	Rationale
Strong	<p>The Guideline Development Group is confident that the desirable effects of adherence to the recommendation outweigh the undesirable effects.</p> <p>With strong recommendations, the guideline communicates the message that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that, in most situations, the recommendation can be adopted as policy.</p>
Conditional	<p>The Guideline Development Group concludes that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects. However, the recommendation is only applicable to a specific group, population or setting or where new evidence may result in changing the balance of risk to benefit or where the benefits may not warrant the cost or resource requirements in all settings.</p> <p>Conditional recommendations are made when there is greater uncertainty about the benefits versus risks, values and preferences, feasibility and acceptability and cost, or if local adaptation has to account for a greater variety in values and preferences or when resource use makes the intervention suitable for some locations but not for others. This means that substantial debate and involvement of stakeholders are needed before this recommendation can be adopted as policy.</p>
No recommendation	<p>Further research is required before any recommendation can be made.</p>

## Cost Analysis

The cost of options available to health-care workers in various settings was not formally assessed because of a lack of primary data in the literature or elsewhere. However, the Guideline Development Group considered the cost implications as part of the general discussion. Comments were therefore restricted to personal experiences and extrapolations from general cost considerations of programmes.

## Method of Guideline Validation

External Peer Review

Internal Peer Review

## Description of Method of Guideline Validation

Members of the External Peer Review Group were asked to review the recommendations developed by the Guideline Development Group to ensure that there were no important omissions, contradictions or inconsistencies with scientific evidence or programmatic feasibility and to assist in clarifying the language, especially in relation to implementation and how policy-makers and programme staff might read them.

No additional recommendations were invited from the External Peer Review Group. The WHO Steering Committee collated the queries raised by the External Peer Review Group and discussed them with the chairs to resolve any inconsistencies or contradictions raised.

The WHO Steering Committee reviewed all suggestions and incorporated the comments as appropriate following discussion and agreement with

the chair and co-chair of the Guideline Development Group. No new recommendations were considered in this round of comments. The Guideline Development Group approved the final version.

## Evidence Supporting the Recommendations

### Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

The available evidence comprised three primary systematic reviews.

## Benefits/Harms of Implementing the Guideline Recommendations

### Potential Benefits

- Extending the period of breastfeeding to 24 months or beyond is likely to improve human immunodeficiency virus (HIV)-free survival among HIV-exposed infants, especially where diarrhoea and pneumonia are significant causes of infant and child mortality; that is, settings with a significantly increased risk of infant and child mortality associated with replacement feeding compared with exclusive breastfeeding. Several other health outcomes among young children and mothers, such as improved child development and reduced maternal breast and ovarian cancer, are also likely to improve as a result of longer duration of breastfeeding.
- Harmonizing the recommendations for HIV-exposed infants and children with those for non-exposed infants would lead to programmatic simplification and facilitate the protection, promotion and support of optimal infant feeding practices in the entire population. Harmonizing the recommendations may also reduce the stigma towards mothers living with HIV associated with stopping breastfeeding early in communities where continued breastfeeding to 24 months or beyond by mothers without HIV is normative.
- Interventions are likely to improve the quality and duration of breastfeeding and therefore the health outcomes of infants, children and mothers.
- Interventions to improve feeding practices among mothers living with HIV are also likely to improve breastfeeding practices in the general population not affected by HIV.
- The Guideline Development Group considered it likely that properly designed counselling and support interventions could simultaneously improve antiretroviral therapy (ART) adherence and retention in care among mothers living with HIV.
- Compared with non-breastfeeding (replacement feeding) in resource-limited settings, mixed feeding in the first six months of life (more correctly referred to as partial breastfeeding) is associated with reduced morbidity among both HIV-exposed and unexposed infants.
- Antiretroviral (ARV) drugs significantly reduce the risk of postnatal transmission – and appear to be effective when mothers living with HIV either exclusively or partly breastfeed. They also appear to be equally effective in reducing HIV transmission after six months of age when complementary foods are introduced, based on supportive evidence that ARV drugs reduce the transmission risks in the context of mixed feeding among infants younger than six months of age.
- Clear messaging and supportive interventions in health services and activities in communities can promote and support exclusive breastfeeding in the general and HIV-exposed populations to achieve the best health outcomes (non-HIV-related) for mothers living with HIV and their infants.
- In the context of maternal ART, low-quality evidence shows that the HIV-free survival of infants born to mothers living with HIV who are breastfed is better than for infants who are never breastfed.
- More closely aligning the recommendations for mothers living with HIV with those for mothers without HIV is likely to improve practices across all populations.

See the "Benefits and Harms" sections in the original guideline document for details on the balance of benefits and harms of specific recommendations.

### Potential Harms

- If maternal antiretroviral therapy (ART) adherence is inconsistent, the potential for human immunodeficiency virus (HIV) transmission increases. In settings where health systems do not reliably provide ART and where maternal adherence is not high, this may result in

transmitting HIV to children who are breastfeeding.

- Compared with exclusive breastfeeding, mixed feeding is associated with a greater risk of serious morbidity, such as diarrhoea and pneumonia and the related mortality among HIV-exposed infants and children. In the absence of ART, it is also associated with an increased risk of postnatal transmission of HIV. However, compared with non-breastfeeding (replacement feeding) in resource-limited settings, mixed feeding in the first six months of life (more correctly referred to as partial breastfeeding) is associated with reduced morbidity among both HIV-exposed and unexposed infants.
- Promoting breastfeeding and antiretroviral (ARV) drugs when mixed feeding is common may appear to endorse mixed feeding and undermine the principle of exclusive breastfeeding.
- There are potential adverse effects on infant growth and other health outcomes associated with longer ARV drug exposure through breast milk. However, the limited data available have not demonstrated such adverse effects.

See the "Benefits and Harms" sections in the original guideline document for details on the balance of benefits and harms of specific recommendations.

## Qualifying Statements

### Qualifying Statements

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## Implementation of the Guideline

### Description of Implementation Strategy

#### Dissemination

The current guideline will be posted on the World Health Organization (WHO) Web site, including the child health, human immunodeficiency virus (HIV) and nutrition Web sites ([http://www.who.int/maternal\\_child\\_adolescent/](http://www.who.int/maternal_child_adolescent/) , <http://www.who.int/HIV> , <http://www.who.int/nutrition/> , the WHO e-Library of Evidence for Nutrition Actions (eLENA) , and social media.

The recommendations in this guideline will be disseminated through a broad network of international partners, including WHO country and regional offices, health ministries, WHO collaborating centres, other United Nations agencies and nongovernmental organizations. They will also be published on the WHO Web site as well as the Web sites of partner agencies. To ensure that the guideline reaches users most likely to benefit from it, WHO will organize meetings among key stakeholders in settings with a high prevalence of HIV and make presentations in international acquired immunodeficiency syndrome (AIDS) and infant feeding conferences. As needed, assistance will be provided to adapt the guideline to national contexts.

The Guideline Development Group specifically commented that it would be important to clarify what changes were included in the recommendations and to comment on what had not changed. They also commented that communities need to be supported in understanding the recommendations and that this would involve simplifying messages. As part of this, coordinating with other health programmes will be essential, including HIV programmes on antiretroviral (ARV) drugs as well as general maternal and child health programmes.

## Adaptation and Implementation

The first steps in implementation after the final approval of this guideline will be to revise all WHO publications that deal with the populations of pregnant women, mothers and infants for whom there may be implications. These include WHO training and reference materials such as: *Integrated management of childhood illness; Infant and young child feeding counselling: an integrated course; Essential newborn care course; Pregnancy, childbirth, postpartum and newborn care: a guide for essential practice* ; *Caring for the newborn at home*; and *Caring for newborns and children in the community: training courses for community health workers*.

WHO will work with health ministries and established partners who are involved with training and capacity development related to HIV and infant feeding and supervision of health workers at first-level health facilities. The successful introduction of evidence-informed policies related to supporting infant feeding practices by mothers living with HIV into national programmes and health-care services depends on well planned and participatory consensus-driven processes of adaptation and implementation. These processes may include developing or revising existing national guidelines or protocols based on this document and also undergraduate and in-service teaching curricula.

Individual countries are expected to adapt the recommendations to suit the local social, cultural and economic contexts. Countries will be encouraged to hold key stakeholder discussions to inform the decision-making on using and introducing the recommendations into national programmes. Frameworks for assisting policy-makers, such as DECIDE (Developing and Evaluating Communication Strategies to Support Informed Decisions and Practice based on Evidence), will be shared. The recommendations contained in the present guideline should be adapted into locally appropriate documents to meet the specific needs of each country and health service.

An enabling environment should be created for the use of these recommendations, including relevant national policies and changes in the behaviour of health-care practitioners to enable the use of evidence-informed practices.

Local professional societies may play important roles in this process, and an all-inclusive and participatory process should be encouraged. WHO's Department of Maternal, Newborn, Child and Adolescent Health, Department of Nutrition for Health and Development, and Department of HIV have substantial experience with introducing WHO guidelines and tools into national programmes.

Within this context, programme managers will need to ensure that adequate quantities of required ARV drugs are available to health workers and mothers living with HIV. These drugs would normally be provided through existing health system supply chains.

### Monitoring and Evaluating the Implementation of the Guideline

Monitoring and evaluation should be built into the implementation process to provide important lessons for uptake and further implementation. For monitoring and evaluating their impact on the quality of care, priority should be given to the strong recommendations.

The implementation of this guideline should involve national child health programmes collecting and reporting data on pregnant women and mothers living with HIV and their exposed newborns. Putting this into practice may require reviewing existing patient monitoring systems, including reporting tools, to ensure that the conditions are adequately addressed.

Key areas that require monitoring include but are not limited to:

- Infant feeding practices by mothers living with HIV, including the duration of breastfeeding
- Antiretroviral therapy (ART) coverage among mothers living with HIV
- Growth among the infants and children being breastfed by mothers living with HIV who are taking ART

The WHO Department of Maternal, Newborn, Child and Adolescent Health, Department of Nutrition for Health and Development, and Department of HIV will monitor the implementation of the guideline in collaboration with WHO regional and country offices using indicators such as the number of requests from countries for technical assistance in implementing the guideline as well as requests to WHO headquarters and regional offices for monitoring and evaluation in countries applying the guideline. In addition, the Department of Maternal, Newborn, Child and Adolescent Health, Department of Nutrition for Health and Development, and Department of HIV will monitor the number of downloads of the guideline publication from the WHO Web site and those of partners and other stakeholders as well as the number of hard copies of the guidance requested and distributed through the WHO document centre.

See also the "Implementation Considerations" subsections in the "Evidence and Recommendations" sections of the original guideline document.

## Implementation Tools

Quick Reference Guides/Physician Guides

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Living with Illness

Staying Healthy

## IOM Domain

Effectiveness

Patient-centeredness

## Identifying Information and Availability

### Bibliographic Source(s)

World Health Organization (WHO), United Nations Children's Fund (UNICEF). Guideline: updates on HIV and infant feeding: the duration of breastfeeding, and support from health services to improve feeding practices among mothers living with HIV. Geneva (Switzerland): World Health Organization (WHO); 2016. 58 p. [52 references]

### Adaptation

Not applicable: The guideline was not adapted from another source.

### Date Released

2016

### Guideline Developer(s)

World Health Organization - International Agency

### Source(s) of Funding

Grants from the United States Agency for International Development, the United States Centers for Disease Control and Prevention and the United States President's Emergency Plan for AIDS Relief supported the development of this publication. The World Health Organization (WHO) also thanks the Bill & Melinda Gates Foundation for financial support for finalizing the guideline document. WHO and the United Nations Children's Fund (UNICEF) are grateful to all the individuals and institutions that contributed time and made other in-kind contributions to the guideline development process. Donors do not fund specific guidelines and do not participate in any decision related to the guideline development process, including the composition of research questions, membership of the guideline groups, conduct and interpretation of systematic reviews or formulation of recommendations.

# Guideline Committee

Guideline Development Group

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## Financial Disclosures/Conflicts of Interest

### Managing Conflicts of Interest

All members of the Guideline Development Group, systematic review teams and members of the External Peer Review Group were required to sign and submit a declaration of interests prior to their participation in the meetings. The World Health Organization (WHO) Steering Committee reviewed the declarations before the Guideline Development Group meeting to determine whether any of the proposed members had a conflict of interest that might have precluded or limited his or her participation. Although the WHO Steering Committee did not identify any conflicts of interest requiring any action, the potential conflicts of interest declared by the Guideline Development Group members are summarized in the "Managing Conflicts of Interest" section in the original guideline document.

## Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: World Health Organization (WHO). Guidelines on HIV and infant feeding. Geneva (Switzerland): World Health Organization (WHO); 2010. 49 p. [47 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Guideline Availability

Available from the [World Health Organization \(WHO\) Web site](#) .

## Availability of Companion Documents

The following is available:

- WHO handbook for guideline development. 2nd edition. Geneva (Switzerland): World Health Organization (WHO); 2014. 167 p.  
Available from the [World Health Organization \(WHO\) Web site](#) .
- Chikhungu L, Bispo S, Newell ML. HIV-free survival at 12–24 months in breastfed infants of HIV-infected women on ART: a systematic

review. Geneva (Switzerland): World Health Organization (WHO); 2016. 36 p. Available from the [WHO Web site](#) .

- Chikhungu L, Bispo S, Newell ML. Postnatal HIV transmission rates at age six and 12 months in infants of HIV-infected women on ART initiating breastfeeding: a systematic review of the literature. Geneva (Switzerland): World Health Organization (WHO); 2016. 31 p. Available from the [WHO Web site](#) .
- Handu D, Acosta A, Moloney L, Wolfram T, Ziegler P, Steiber A. Systematic review of effectiveness of interventions to promote exclusive breastfeeding in women that are HIV (+) on anti-retroviral therapy living in areas that promote exclusive breastfeeding due to limited resources for safe replacement feeding. Chicago (IL): Academy of Nutrition and Dietetics; 2016. 54 p. Available from the [WHO Web site](#) .
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- Sinha B, Chowdhury R, Sankar MJ, Martines J, Taneja S, Mazumder S, Rollins N, Bahl R, Bhandari N. Interventions to improve breastfeeding outcomes: a systematic review and meta-analysis. Acta Paediatr. 2015 Dec;104(467):114-34. Available from the [Acta Paediatrica Web site](#) .

An executive summary is available in the [original guideline document](#) .

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on August 9, 2012. This summary was updated by ECRI Institute on January 30, 2017.

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